

WILLIAM J. KERR, M. D. (University of California Medical School, San Francisco).—In discussing the paper by Doctor Newman and Doctor Spiro on the use of quinidin in auricular fibrillation I find it somewhat difficult to give an estimate of the value of this work without knowing a little more about how patients were selected for treatment. The high percentage of successful results in terminating the attacks of auricular fibrillation suggests that a good deal of selection was made before treatment was started. The results, therefore, are not comparable with those reported by others unless we know how many patients were seen during this time who were excluded from the series and more about the criteria upon which the patients treated were selected for this purpose. In our own clinic we have had approximately the same percentage of successful results in auricular fibrillation, but have excluded from treatment a great many patients who would have been included in earlier series.

It is somewhat difficult to say anything about the statistical results reported by these authors. The authors state that they would not use quinidin in patients over sixty-five years of age, but do not offer any real proof that there is great danger in this group. It seems to me that it is one of the most valuable drugs for many of our old people who are beginning to show paroxysmal auricular fibrillation or have auricular fibrillation develop during the course of an infection or following an operation. It is quite certain that in many of these cases quinidin will not maintain a normal rhythm, but it seems to be of very great value in tiding some of these older people over a critical period. With regard to quinidin in general, it seems to me that if one can restore the normal sinus rhythm the patients are usually more comfortable than they were with auricular fibrillation. The only exceptions to this are those cases where the patient develops a tachycardia which may be the cause of more discomfort than the patient experiences from the auricular fibrillation. I think if one can restore the normal sinus rhythm and maintain it for a period of a few months that the treatment is worth while. So often the onset of one of the irregularities seems to herald a general circulatory failure, and if the irregularity can be stopped, then the prognosis seems a little bit more hopeful.

The dangers in the use of quinidin are to be kept in mind. We must remember that quinidin is a powerful drug and that if we are to give it until we secure some effects from it, there will be cases where toxic effects will appear. These, fortunately, are usually transient, but occasionally may be very serious. Embolism, of course, is one of the accidents which may occur during treatment or when the sinus rhythm is restored, but we must remember that it is in that same group of cases that embolism occurs with digitalis or without any treatment at all. It is doubtful whether the quinidin should really be blamed for many of these accidents. Physicians should learn how to use this drug just as they have to learn how to use morphin, digitalis, and other potent drugs.

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DOCTOR SPIRO AND DOCTOR NEWMAN (Closing).—We wish to thank Dr. Manning Clarke for his very kind appreciation of our paper. We consider the estimation of the vigor of the heart's pulsatory waves as seen fluoroscopically as one of the most important points in judging whether sufficient cardiac compensation has been restored to make the attempt at restoration of sinus rhythm with quinidin fairly safe.

Doctor Kerr states that in his clinic he has about the same percentage of cures of auricular fibrillation as we have had. He wishes to know more of the reasons for our conclusions why we do not approve of the use of quinidin in patients with chronic auricular fibrillation if the patient is over sixty-five years of age. In the text of our paper we stated that none of our patients over sixty-five years maintained a

normal restored rhythm for a sufficient length of time to have warranted the danger incurred, and that one-half of the patients over sixty-five years died twenty-four hours after the restoration of normal rhythm.

We concur in Doctor Kerr's opinion that the physician should learn the proper method of using quinidin, but we who have been enthusiastic, even to the point of recklessness in the use of quinidin, are now attempting to give the medical profession the benefit of a safer and saner road to follow.

Among other subjects, Doctor Kerr speaks of paroxysmal auricular fibrillation. We beg leave to state that that subject was not under discussion. We agree to the use of quinidin for paroxysmal auricular fibrillation for any aged patient except those suffering from acute coronary artery occlusion, in which event we maintain that digitalis is the proper treatment.

## THYROTOXICOSIS—END RESULTS IN ITS ROENTGEN TREATMENT\*

By J. MARION READ, M. D.  
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DISCUSSION by William J. Kerr, M. D., San Francisco;  
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THE material which forms the basis of this report is a follow-up study of thyrotoxic patients seen in the nine years, 1920 to 1928 inclusive. The reason no cases which have come under observation in the past three years are included in this series is because it was my endeavor to ascertain the late results of roentgen irradiation, that is, the condition of these patients three to eleven years after treatment. The impression seems to be widespread among those who favor surgical removal that irradiation of the thyroid is only palliative and seldom results in permanent cure. It is this point, particularly, upon which I hope to throw some light.

### MATERIAL FOR THIS STUDY

Roentgen ray and general journals contain a great many statistical reports of the use and results of roentgen irradiation in thyrotoxicosis, and one more communication would merely seem like reaffirming what is, or should be, already generally known. Particularly, in view of the recent complete and excellent reports by Pfahler and Vastine<sup>1</sup> in this country and Holzknecht<sup>2</sup> in Germany, an additional report would only gild the lily unless some additional factors are incorporated. To secure additional data I re-examined as many former patients as I could reach and persuade to return for a complete examination. Anyone who has attempted to get in communication with patients seen five to ten years previously will appreciate the difficulties. I therefore have no apologies to make for the small per cent of former patients I was able to re-examine, believing that the time element and the fact that most of them were seen and examined personally compensates for their small number.

\* Read before the Radiology Section of the California Medical Association at the sixtieth annual session at San Francisco, April 27-30, 1931.

I may add here that in addition to an interval history, a basal metabolic rate determination and examination for residual signs for thyrotoxicosis, I also endeavored to determine the integrity of the cardiovascular system. Each patient's heart was examined, blood pressure recorded, functional test made and electrocardiogram taken. A teleroentgenogram was also taken to determine heart size accurately. Only the general results of these examinations will be given here, as it is intended to make a detailed report on the cardiovascular system in thyrotoxic patients at a future time.

#### BASIS OF SELECTION FOR ROENTGEN THERAPY

This series does not embrace all thyrotoxic patients seen during the period covered because every such patient is not irradiated. Although all patients reported here had roentgen-ray therapy, each received also other treatment, including rest, forced feeding, iodine, sedatives, and such symptomatic therapy as seemed suited to his individual need.

In anticipation of the question, "Which patients are given roentgen-ray treatments?" I will reply that it is used in those patients who do not respond quickly and satisfactorily to other measures. I should add that since iodine has received general sanction I have found irradiation necessary in fewer cases than it was prior to 1924. I do not know, and I am not aware that anyone is prepared to tell us just what irradiation does to the thyroid, but empirically it produces amelioration of symptoms and objective improvements that can be measured quantitatively by a fall in the basal metabolic rate. I use irradiation as I do surgery, specifically in the more severe and resistant cases and believe that its effect differs from that of surgery in degree only. The roentgen ray accomplishes, temporarily and without risk, what surgery aims to produce permanently, namely, a reduction in toxicity and in basal metabolic rate. Experience has led me to the opinion that irradiation is no more a cure for Graves' disease than is surgery. I harbor no delusions, therefore, as to the ultimate curative value of this form of treatment, having been convinced years ago that thyrotoxicosis, especially the Graves' syndrome, runs a fairly definite course over a period of approximately one and a half to three years. Our therapeutic endeavors, including x-ray and surgery, may alter this course somewhat, but do not greatly shorten it and do not by themselves produce a cure. This viewpoint and the reasons for arriving thereat I set forth in the *Journal of the American Medical Association* in 1924.<sup>3</sup>

To correctly evaluate any therapeutic measure employed in the course of a self-limited disease is exceedingly difficult, if not impossible. I shall, therefore, not attempt it here. Upon numerous occasions I have already pointed out the peculiar power which the "post hoc, ergo propter hoc" fallacy exerts over the minds of therapists

when discussion of thyrotoxicosis is their theme. I do not propose, therefore, to fall into this pit myself. I simply report here the results in a series of cases in which irradiation was used, believing that the results themselves are sufficient to justify the inclusion of irradiation in the list of therapeutic measures directed against thyrotoxicosis.

#### ADEQUATE DOSAGE

Since adequate dosage is essential in every case except in those who would recover anyway without any treatment, I will define what has proven adequate in our experience. During the past eleven years the technical factors involved in the roentgen treatments have changed considerably. In general it would be fair to say that the average patient received weekly radiations over each lobe of approximately 200 r. The ray was usually generated at 130 kilovolts, the beam being filtered through .25 millimeter of copper and 1 millimeter of aluminum. Twelve such treatments constituted a full course, only a few patients being given more than one such course in a year. In several obstinate cases a shorter, but similar, course was given in the second year.

#### REPORT ON FIFTY PATIENTS TREATED PRIOR TO 1928

In 1924 I reported the cases of fifty thyrotoxic patients treated by roentgen ray.<sup>4</sup> The present report embraces, in part, a follow-up study of such of that former series as could be located after an interval of seven to eleven years. In addition there are seven cases from patients treated between 1924 and 1928.

In a follow-up series to ascertain the effect of roentgen ray it seems advisable to exclude all cases where surgery has also been performed, since the extravagant claims made for surgery would almost certainly lead its proponents to claim all credit for any improvement which the patient showed.

Therefore from the 1924 series of fifty I would exclude five who had been thyroidectomized prior to being irradiated. Two of these are known to be alive, one of whom takes thyroid extract for her myxedema. A third patient could not be located. The fourth must be classed as both a surgical and x-ray failure, as she had a basal metabolic rate of plus 80 per cent four years after operation and after a year's treatment, including x-ray, the rate was plus four per cent, but she was not cured. She still had all the nervousness characteristic of true Graves' disease, and one day in her confusion she stepped in front of a street car and thus met her end. The fifth submitted to a second thyroid operation and died in three months from myxedema and tetany.

Seven of the series were operated upon shortly after being irradiated, the roentgen-ray therapy being used in preparation for surgery, or being considered a failure after a month or two of irradiation.

TABLE 1.—Late Results in the Treatment of Thyrotoxicosis

No.	Name	Age	First B. M. R.	Irradiations		Months Observed	Discharge		Time Since Discharge	Present Age	B. M. R. %	End Result
				No.	Approximate r. to Each Lobe		B. M. R.	State				
1	Mrs. E. B.	34	+23	....	.....	3.5	+2	Impr.	10 yrs. 2 mos.	44	-4	Cured
2	Mrs. M. D.	45	+112	21	6090	20.0	+8	Impr.	6 yrs. 10 mos.	54	-2	Cured
3	Mrs. H. C.	41	+67	12	3200	3.5	+6	Cured	9 yrs.	50	-3	Cured
4	Mrs. C.	60	+60	8	4230	9.3	+17	Impr.	7 yrs. 6 mos.	69	+2	Cured
5	Mrs. R. B.	32	+42	3	1440	2.4	-7	Cured	7 yrs. 8 mos.	39	-1	Cured
6	Mrs. B. M.	28	+42	4	?	26.0	+25	Impr.	5 yrs. 6 mos.	35	-1	Cured
7	Mrs. B. S.	48	+45	3	795	4.0	.....	Cured	7 yrs. 6 mos.	55	+4	Cured
8	Mrs. J. G.	46	+45	23	2300	32.0	+46	Chronic	7 yrs.	55	+7	Cured
9	Mr. K. S.	37	+66	14	4000	28.0	-10	Cured	4 yrs. 9 mos.	43	-6	Cured
10	Mrs. A. F.	43	+54	5	1140	26.6	+11	Impr.	1 yr.	46	+10	Chronic
11	Mrs. G. B.	49	+55	8	800	24.0	.....	Impr.	4 yrs.	55	+27	Chronic
12	Miss E. R.	12	+40	12	2850	3.0	+12	Cured	4 yrs. 10 mos.	17	.....	Cured
13	Mr. R. S.	43	+65	6	?	7.0	+49	Impr.	6 yrs.	50	.....	Chronic
14	Miss C. H.	42	+62	3	600	32.0	+32	Impr.	4 yrs. 3 mos.	49	.....	Cured
15	Mrs. F. S.	27	+23	5	?	22.0	+14	Impr.	2 yrs.	31	+24	Chronic
Average		39	+53			15.6	+15		6 yrs.	46	+5	

Eliminating these thirteen who received also surgical treatment, there remain thirty-seven, of whom one is known to have died of malignant hypertension. Of the other thirty-six I have been able to secure follow-up data on eight who reported in person for re-examination.

The detailed results of this study are shown in Table 1, and it is only needful to mention here the chief features and present two illustrative cases. Final results of treatment are given in two categories only—"cured" and "chronic," this latter designation implying that treatment failed. The severest criteria were used in judging the results. Every patient whose metabolic rate was not within normal limits or who had any residual signs or symptoms was classed as uncured.

Of the eight cases from the 1924 series, three were reported at that time as cured, four as improved, and one showed no change. The first three have remained well, and none has suffered a remission. But what is still more gratifying, this follow-up study reveals that the other five are now well, after an average elapsed time of seven years. It seems fair to assume that most, if not all, of the more recent group, designated now as "chronic," will completely recover also.

#### HISTORY OF TWO CASES

CASE 1.—The history of Mrs. M. D., considered only improved at the time of discharge seven years ago, is instructive. Because of certain interesting features her history up to 1924 was reported in detail in "Endocrinology,"<sup>5</sup> and only the briefest summary is presented here, with a record of her present status.

When first seen in July 1922, aet. forty-five, she gave a history which indicated an onset of thyrotoxicosis in 1915, although thyroid enlargement was not observed until 1917. Her symptoms increased until March 1922, at which time she had lost forty pounds. By May she had to go to bed because of weakness and vomiting. Christian Science leanings inhibited her from receiving continuous medical attention. In July 1922 she weighed 110 pounds, had a large, soft, vascular thyroid, exophthalmus, marked tremor, extreme weakness, and a pulse rate of 132. At that time she presented the most extreme picture of thyrotoxicosis I have ever

seen, short of terminal thyroid crises. A determination of the basal metabolic rate gave the result of plus 112 per cent. Because of her extreme weakness, tremor and nervousness, this was only an approximation, but not far from correct, as one month later, when she was considerably improved, the rate was plus 80 per cent and remained at this level for yet another month. She remained in the hospital for two months and in bed for six months, receiving symptomatic medication and weekly roentgen irradiations with gradual improvement which continued for twenty months, with recurrences at nine and seventeen months, the metabolic rate in these reaching as high as plus 40 per cent.

In March 1924 her metabolic rate was plus eight per cent, but she still had tremor, easy fatigability and exophthalmus, and showed signs of congestive heart failure.

When seen in January 1931 she presented the picture of a perfectly healthy woman of fifty-four years, pulse rate 68, basal metabolic rate minus two per cent, weight 148 pounds, and without subjective or objective manifestations of thyrotoxicosis. Her feet no longer swelled, physical examination, electrocardiogram, and teleroentgenogram revealed no cardiac pathology.

CASE 2.—One other case history is given here for two reasons: first, the patient was diagnosed as having a toxic adenoma; and secondly, hers is the case in which roentgen irradiation and all other nonsurgical treatment was considered a failure.

Mrs. J. F. B., housewife, forty-five years of age, was first seen in September 1921, when she gave a history of nervousness and weakness beginning in January of that year. Her basal metabolic rate was plus 46 per cent at this time and she presented manifestations of thyrotoxicosis in keeping with this rate. The thyroid was only slightly enlarged, firm, and thought to be nodular.

She had lived in the endemic goiter district of the Pacific Northwest from the age of thirteen until just prior to coming under our observation. She stated that "her whole family had large thyroids." This history, perhaps more than the physical findings, led to a diagnosis of toxic nodular goiter rather than Graves' disease, although there were none of the classical eye signs present.

Of importance in her history was her statement that in 1910 a physician was consulted in Spokane because of palpitation. He gave bromids and told her he wanted to take an x-ray picture of her throat. Also early in 1921 another physician told her that her blood pressure was 190.

Her subsequent course for two and one-half years, as measured by objective methods, is shown in Fig. 1. At one examination there was detected a cardiac irregularity which the electrocardiogram revealed was due to progressive heart block in which every sixth or seventh beat was blocked. For nine months in 1921 there was suppression of menses, not due to pregnancy.

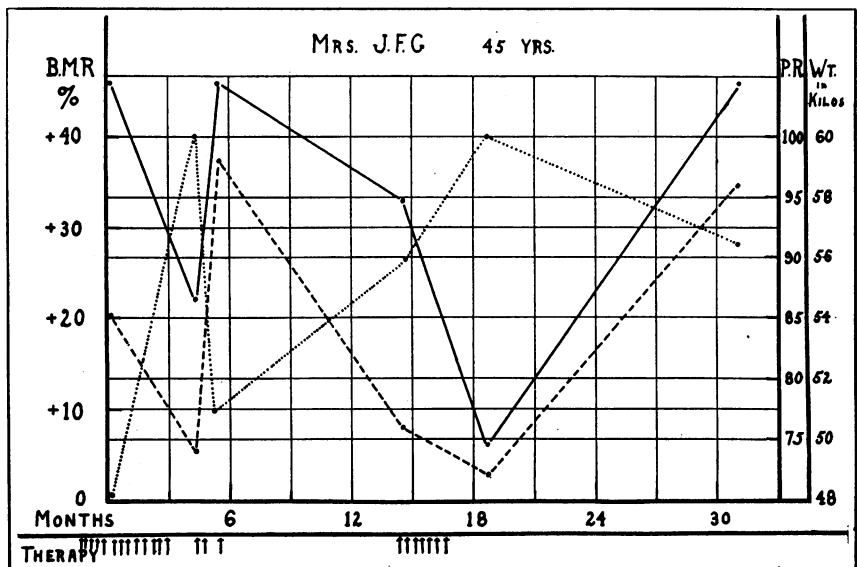


Fig. 1.—Course for thirty-one months of a thyrotoxic patient believed to have a nodular goiter. Solid line, basal metabolic rate; broken line, pulse rate; dotted line, weight. Arrows in row marked "Therapy" indicate x-ray treatments.

When seen for a follow-up examination on March 31, 1931, she stated that she had been feeling fine, was not nervous, and had no palpitation, although these symptoms persisted for three or four years. She does not get tired now and can do things that she had been unable to do for years. Her metabolic rate was plus seven per cent, pulse rate 76 to 80, and blood pressure 180/80. One ectopic beat was noted and she showed other mild signs of cardiovascular disease which accompany hypertension.

This patient, now at the age of fifty-five years, is in very good health though she was diagnosed ten years ago as having a toxic nodular goiter. Either this type is as amenable to roentgen irradiation as the hyperplastic gland of Graves' disease, or else this distinction does not exist. If she had now a nodular goiter I might be led to conclude that she had developed acute Graves' disease coincidental to a nontoxic goiter. It is possible that the customary distinction between Graves' disease and toxic nodular goiter is unjustified, although in the majority of cases it is a useful classification for therapeutic purposes since the latter type of case seems best treated by thyroidectomy, and it is in this type of patient that surgery yields brilliant and permanent results, which cannot be said for Graves' disease. Roentgen irradiation was used in this patient who was believed to have had a toxic nodular goiter, as have had similar patients where surgery was refused or contraindicated, yet these are exceptions, for as a rule I prefer surgery for the typical case of nodular toxic goiter.

In conclusion I wish to point out that none of the four patients classed as "chronic" had adequate roentgen irradiation as I have defined it. This fact is partially evident from the table, but becomes better understood by study of their individual case histories where the manner of their treatment is revealed more specifically. If this

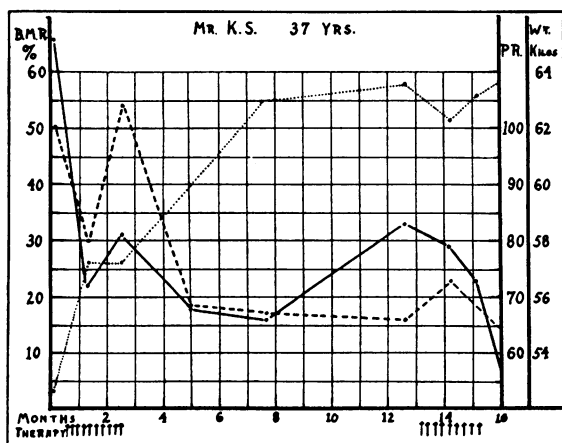


Fig. 2.—Course for sixteen months of a man with classical Graves' disease. Solid, broken and dotted lines, and arrows have same significance as in Figure 1.

study has shown that thyrotoxic patients who received roentgen irradiation get well and remain well, it also reveals that adequate dosage is essential to success. While insisting that radiation therapy be carried out by skilled experts, I also insist that the management of the patient remain in the hands of an internist or the patient's family physician. If credit is to redound to this form of treatment the patients sent to the roentgenologist must be correctly diagnosed, wisely selected and properly handled with respect to symptomatic relief and complications if there be any.

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#### DISCUSSION

WILLIAM J. KERR, M. D. (University of California Hospital, San Francisco).—Doctor Read has brought up a subject which has been of very great interest to me now for several years. It has been almost impossible to bring together the various groups who are interested in the treatment of thyroid disease, as each one feels that his own particular method of treatment surpasses any of the others.

There is no doubt that in selected cases medical treatment alone with rest, diet, and iodine will give very satisfactory results. X-ray treatment alone is very beneficial in a considerable number of cases. The results of surgical removal are very much quicker and more spectacular, but are not necessarily permanent. Furthermore, in the hands of the average surgeon the mortality is still extraordinarily high, whereas with the nonsurgical methods of treatment the mortality is practically nil although there may be prolonged disability and the life of the patient may

be shortened if treatment is not entirely successful. It is my opinion that x-ray treatment, combined with other measures, and especially with very small doses of iodine (one to two drops of Lugol's solution a day over a long period of time), is about as satisfactory as surgical treatment.

We are making a study of patients suffering from thyrotoxicosis and are trying to see all patients who present themselves for treatment and to follow these for a long period of time under various methods of treatment. We are also trying to see personally the patients who have been operated upon during the past years. On our committee we have the departments of pathology, surgery, roentgenology, endocrinology, medicine, and pediatrics represented. It is too early, after a period of over a year, to say what the final conclusions are going to be. We expect to continue this study for many years. However, there are some suggestions that there may be a group of patients where they may be found to respond equally well to any of the so-called standard methods of treatment and there may be another group where no satisfactory results will be obtained with any of these methods. We are all familiar with the occasional case where adequate surgical removal has apparently been carried out and where in succeeding years the part of the gland remaining will become enlarged and active again. In some patients it may be necessary to remove portions of the gland three or four times. Some may say that this is because of inadequate removal in the beginning, but this opinion is probably incorrect.

Doctor Read should be commended on his follow-up studies on his patients and for his comments about adequate dosage. The results of roentgen-ray treatment in thyroid disease are very much better now than they were a few years ago because of improved technique.

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WILLIAM E. COSTLOW, M. D. (1407 South Hope Street, Los Angeles).—Thyrotoxicosis, or hyperthyroidism, being a disease of questionable origin, unfortunately, does not have a specific treatment or cure.

Surgery and radiation are both empiric methods of treatment used to destroy the hyperplastic glandular structure, the latter being used with the idea of decreasing the secretory action of the cells in the gland. Both are really mechanical methods of treatment, and one is as logical as the other. Experience has shown that amelioration of symptoms and objective improvement have occurred following each method of treatment. Failures have also occurred following each method of treatment. Reliable statistics show that both methods have about the same percentage of cures, 65 to 70 per cent.

Improvement in the percentage of radiation cures was brought about in the past few years by the improvement in radiation technique. Higher voltages have been used, with heavier filtration, insuring adequate depth dosage throughout the thyroid tissue. In our experience it has been necessary to give somewhat larger total dosages than those outlined by Doctor Read, in order to secure permanent results. Some patients require quite prolonged irradiation, repeated at intervals over six months or one year. It is often two or three months before any beneficial effects appear following radiation.

In view of the present-day evidence of an increasing percentage of reliable radiation cures, it is certainly justifiable to advise radiation in properly selected thyrotoxic cases. Should radiation fail, surgery may still be carried out, as the surgical risk is not increased, but may even be decreased, because the metabolic rate and toxic symptoms may be lessened.

The advice that radiation treatments should be skillfully given is important, as is also the idea that during treatment the skillful management of the internist is indispensable.

We believe Doctor Read's finding, that some of his patients originally reported as only "improved" but not completely cured, and found to be completely cured after an average elapsed time of seven years, is rather a common observation in irradiated cases of thyrotoxicosis. We have observed a number of similar cases in our clinic.

Apparently none of the four patients in Doctor Read's table classed as "chronic" received adequate roentgen dosage. As all of these patients showed improvement, additional dosage would probably have produced permanent relief. One patient who showed a reduction in metabolism from plus 54 to plus 10 had received only 1140 r and was only under observation one year. Another patient was reduced from plus 55 to plus 27, although she only received a total of 800 r, which is usually an entirely inadequate total dosage.

Doctor Read's paper again demonstrates clearly and very scientifically that thyrotoxic patients who receive adequate radiation dosage do get well and remain well.

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JOHN HUNT SHEPARD, M. D. (Medico-Dental Building, San Jose).—It is from such reports as Doctor Read has given us, based on years of careful observation, that medical knowledge is increased.

Patients afflicted with Graves' disease have returned to health after receiving most varied kinds of treatment or no treatment at all, and therefore it becomes most difficult to evaluate properly any form of treatment unless the response to it is prompt and definite.

I cannot become enthusiastic over irradiation in thyrotoxicosis when one patient returns to health after receiving a dosage of but 200 r to each lobe of the thyroid gland while another will receive 4000 r, or more, over a period of many weeks or months with little or no abatement of symptoms. Although irradiation in Graves' disease has been used for many years, and we have heard a great deal about "adequate dosage," we have been given no definite information as to what is adequate.

In CALIFORNIA AND WESTERN MEDICINE, July 1925, I wrote "... it is irrational to destroy a portion of any factor to curtail its output ..." but when we do a subtotal thyroidectomy, leaving glandular tissue equivalent in volume to one-fourth the amount of a normal thyroid gland, at least 75 per cent of our thyrotoxic patients return to normal health within six months, and of those upon whom we operate within two months of the onset of their symptoms, the percentage of cures is higher and the time required for complete relief of symptom is shorter.

Those favoring nonsurgical treatment of thyrotoxicosis seem to keep before their minds the so-called surgical fatalities and postoperative myxedema and tetany. A careful study of the records of these surgical failures show that the vast majority are analogous to the records of patients with appendicitis when they were given the benefit of four or five days' treatment before operation, and though we all have seen patients recover from an attack of appendicitis under nonsurgical treatment and occasionally have seen a patient die following an early simple appendectomy, most of us agree that early surgical intervention is the proper procedure.

As I wrote in 1925, "I look forward to the time when thyroidectomy will not be the treatment for this disease, ..." but in the light of our present knowledge greater success is obtained by a properly performed thyroidectomy than by any other treatment.

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DOCTOR READ (Closing).—It seems quite fitting that an internist, a roentgenologist, and a surgeon should discuss this paper for, as Doctor Costolow reminds

us, this is a disease of questionable or unknown etiology for which there is no specific treatment, and its proper handling often requires the coöperation of several specialists. The plan of study outlined by Doctor Kerr should broaden the viewpoint of every physician who participates in the conference long enough to obtain late follow-up data. Doctor Kerr intimates that they are demonstrating that the same is true of thyrotoxicosis that is true of almost every other disease, namely, there are some patients who recover with any or no treatment, and at the other extreme there are a few which resist every form of therapy. A very similar viewpoint was expressed upon this subject by me in 1926 (February) in the *American Journal of the Medical Sciences*.

I am grateful to Doctor Costolow for emphasizing again that beneficial results may not follow until two or three months after institution of treatment, and that it is necessary in some patients to repeat the treatments in six to twelve months. He has pointed out the tendency toward using heavier dosage, which is the crux of the matter in successful irradiation for thyrotoxicosis. What constitutes adequate dosage in any given case is difficult to determine, but we have progressed to the point where we are sure a patient has not been adequately treated until he has been given much heavier dosage than it has been customary in the past. We cannot, therefore, enlighten Doctor Shepard as to what constitutes "adequate dosage" and we are as much in the dark as to what constitutes "a properly performed thyroidectomy." Many such operations which seemed properly performed have not been attended by the anticipated results.

### CINCHOPHEN ADMINISTRATION— JAUNDICE AS AN UNTOWARD EFFECT\*

#### REPORT OF CASES

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FOLLOWING the introduction of cinchophen into materia medica by Nicolaier and Dohrn<sup>1</sup> in 1908, its use became widespread owing to its remarkable pain-relieving properties in arthritic and neuritic conditions. For fifteen years its reputation was unassailed, except by an occasional report of a minor toxic manifestation. However, Worster-Drought<sup>2</sup> in 1923 reported a case of severe jaundice following the ingestion of atophan. Cabot<sup>3</sup> in 1925 described a case of fatal poisoning by a preparation (weldona) containing cinchophen. The necropsy showed an extensive parenchymatous degeneration of the liver. Since the appearance of Cabot's report a number (thirty-two) of fatal cases of cinchophen poisoning have appeared in the literature. Postmortem examination of these cases has invariably demonstrated severe liver damage characterized by

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